

### Amendments to the Specifications

Please replace paragraph 0007 with the following paragraph:

[0007] Typically, the aerosol has a mass of at least 10  $\mu\text{g}$ . Preferably, the aerosol has a mass of at least 100  $\mu\text{g}$ . More preferably, the aerosol has a mass of at least 200  $\mu\text{g}$ .

Please replace paragraph 0017 with the following paragraph:

[0017] Typically, the condensation aerosol has a mass of at least 10  $\mu\text{g}$ . Preferably, the aerosol has a mass of at least 100  $\mu\text{g}$ . More preferably, the aerosol has a mass of at least 200  $\mu\text{g}$ .

Please replace paragraph 0074 with the following paragraph:

[0074] Diazepam was purchased from Sigma ([www.sigma-aldrich.com](http://www.sigma-aldrich.com)).

### EXAMPLE 1

#### *Volatilization of Diazepam*

Diazepam (10.0 mg) in 120  $\mu\text{L}$  dichloromethane was coated onto a circular piece of aluminum foil (10 cm in diameter). The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the diazepam coating on the 78.5 cm<sup>2</sup> aluminum solid support, after solvent evaporation, is about 1.3 microns. The aluminum foil was secured onto a 100 mm x 50 mm petridish using parafilm. After cooling the glass bottom of the petridish with dry ice, the aluminum side of the apparatus was placed on a hot plate at 240°C for 10 s. The apparatus was removed from the hot plate and allowed to cool. Acetonitrile was injected through the aluminum foil onto the inside of the glass surface using a 3 mL syringe. The acetonitrile solution was concentrated and analyzed by high performance liquid chromatography with UV absorbance detection at 225 nm light, which indicated that the volatilized material was at least 99.9% pure.

Please replace paragraph 0075 with the following paragraph:

## EXAMPLE 2

### *Volatilization of Diazepam Using a Halogen Bulb Heat Source*

[0075] A solution of 5.3 mg diazepam in 120  $\mu$ L dichloromethane was coated on a 3 cm x 8 cm piece of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the diazepam coating on the 24 cm<sup>2</sup> aluminum solid support, after solvent evaporation, is about 2.2 microns. The coated foil was wrapped around a 300 watt halogen tube (Feit Electric Company, Pico Rivera, CA), which was inserted into a glass tube sealed at one end with a rubber stopper. Running 40 V of alternating current (driven by line power controlled by a variac) through the bulb for 17 s afforded diazepam thermal vapor (including diazepam aerosol), which collected on the glass tube walls. Reverse-phase HPLC analysis with detection by absorption of 225 nm light showed the collected material to be at least 99.9% pure diazepam.

Please replace paragraph 0076 with the following paragraph:

## EXAMPLE 3

### *Particle Size, Particle Density, and Rate of Inhalable Particle Formation of Diazepam Aerosol*

[0076] A solution of 18.2 mg diazepam in 200  $\mu$ L dichloromethane was spread out in a thin layer on the central portion of a 4 cm x 9 cm sheet of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the diazepam thin layer on the 36 cm<sup>2</sup> aluminum solid support, after solvent evaporation, is about 5.1 microns. The aluminum foil was wrapped around a 300 watt halogen tube, which was inserted into a T-shaped glass tube. One of the openings of the tube was sealed with a rubber stopper, another was loosely covered with the end of the halogen tube, and the third was connected to a 1 liter, 3-neck glass flask. The glass flask was further connected to a large piston capable of drawing 1.1 liters of air through the flask. Alternating current was run through the halogen bulb by application of 90 V using a variac connected to 110 V line power.

Within 1 s, an aerosol appeared and was drawn into the 1 L flask by use of the piston, with collection of the aerosol terminated after 6 s. The aerosol was analyzed by connecting the 1 L flask to an eight-stage Andersen non-viable cascade impactor. Results are shown in table 1. MMAD of the collected aerosol was 1.74 microns with a geometric standard deviation of 2.02. Also shown in table 1 is the number of particles collected on the various stages of the cascade impactor, given by the mass collected on the stage divided by the mass of a typical particle trapped on that stage. The mass of a single particle of diameter  $D$  is given by the volume of the particle,  $\pi D^3/6$ , multiplied by the density of the drug (taken to be 1 g/cm<sup>3</sup>). The inhalable aerosol particle density is the sum of the numbers of particles collected on impactor stages 3 to 8 divided by the collection volume of 1 L, giving an inhalable aerosol particle density of  $5.87 \times 10^{10}$  particles/L ( $5.87 \times 10^7$  particles/mL). The rate of inhalable aerosol particle formation is the sum of the numbers of particles collected on impactor stages 3 through 8 divided by the formation time of 6 s, giving a rate of inhalable aerosol particle formation of  $9.8 \times 10^9$  particles/second.

Please replace paragraph 0078 with the following paragraph:

#### EXAMPLE 4

##### *Drug Mass Density and Rate of Drug Aerosol Formation of Diazepam Aerosol*

[0078] A solution of 5.1 mg diazepam in 200  $\mu$ L dichloromethane was spread out in a thin layer on the central portion of a 4 cm x 9 cm sheet of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the diazepam coating on the 36 cm<sup>2</sup> aluminum solid support, after solvent evaporation, is about 1.4 microns. The aluminum foil was wrapped around a 300 watt halogen tube, which was inserted into a T-shaped glass tube. One of the openings of the tube was sealed with a rubber stopper, another was loosely covered with the end of the halogen tube, and the third was connected to a 1 liter, 3-neck glass flask. The glass flask was further connected to a large piston capable of drawing 1.1 liters of air through the flask. Alternating current was run through the halogen bulb by application of 90 V using a variac connected to 110 V line power. Within seconds, an aerosol appeared and was drawn into the 1 L flask by use of the piston, with formation of the aerosol terminated after 6 s. The aerosol was allowed to sediment onto the walls of the 1 L flask for approximately 30 minutes. The flask was then extracted with dichloromethane and the extract analyzed

Serial No. 10/792,001

Amendment dated June 01, 2005

Response to Office Action dated December 01, 2004

by HPLC with detection by light absorption at 225 nm. Comparison with standards containing known amounts of diazepam revealed that 3.8 mg of > 99% pure diazepam had been collected in the flask, resulting in an aerosol drug mass density of 3.8 mg/L. The aluminum foil upon which the diazepam had previously been coated was weighed following the experiment. Of the 5.1 mg originally coated on the aluminum, all of the material was found to have aerosolized in the 6 s time period, implying a rate of drug aerosol formation of 0.85 mg/s.